PLAN OF THESIS

MICRONEEDLING VERSUS TOPICAL TAZAROTENE 0.1% GEL FOR THE TREATMENT OF ATROPHIC POST ACNE SCARRING - A RANDOMIZED CONTROLLED STUDY

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SUMMARY OF THE PROPOSED RESEARCH

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit. It manifests clinically as non-inflammatory (open and closed comedones) or inflammatory (papules, pustules and nodules) lesions**.** The major brunt of the disease is borne by adolescents aging 16-20 years as shown by a study in India[1]. Scarring as a sequel to acne can occur in up to 95% of acne patients and 30% may develop cosmetically disfiguring scarring.[2]

Various factors have a role in the causation of acne. The major ones are increased sebum production, hypercornification of pilosebaceous duct, abnormal colonization of pilosebaceous unit by *Propionibacterium acnes* and inflammation. The uninhibited inflammatory process in acne initiate the process of wound healing with the granulation tissue formation and remodeling of extracellular matrix.[3] Depending on the activity and balance between the components involved in the process, there can be a net loss or gain of collagen forming atrophic or hypertrophic scars respectively.[4] Thus the inflammatory process associated with acne lead to post acne scarring.

Jacob et al classified atrophic acne scars as icepick (60%–70%), rolling(15%–25%) and boxcar (20%–30%) depending on their shape.[5] For the ease of identification and stratification of severity, atrophic acne scars are graded by different scales, of which the most popular ones are the qualitative scale and the quantitative scale proposed by Goodman and Baron.[6, 7]

Eventhough acne scarring is permanent, the appearance can be improved with various medical, laser, surgical and tissue augmentation techniques. Topical retinoids are the mainstay of medical management for macular post acne scars. They reduce epidermal melanin by inhibiting the action of tyrosinase and and also by reduction of melanosome transfer to keratinocytes. Retinoids also normalizes keratinocyte differentiation, reduces the inflammation and stimulates collagen synthesis.[8, 9] Topical tazarotene is therapeutically effective as 0.1% gel or 0.1% cream.[10, 11]Tazarotene (0.1%) gel was found to be superior to adapalene (0.1%) and tretinoin (0.025%, 0.1%) for the treatment of acne vulgaris.[12] Based on its mechanism of action and role in collagen

synthesis, topical tazarotene is a logical choice to investigate for the management of atrophic post acne scars.

Among the procedural methods, microneedling with dermaroller is a novel and promising option. It is a minimally invasive procedure for the management of atrophic acne scars.[13] It causes per-cutaneous collagen induction by augmenting the natural process of wound healing.[14] There are studies establishing the efficacy of newer dermatosurgical technique, the microneedling in atrophic post acne scar management.[15, 16] The efficacy of topical tazarotene in the management of acne vulgaris and reducing PIH has been proved in previous published studies.[12, 17]This is a pilot study comparing microneedling and topical tazarotene for the treatment of atrophic post acne scarring in regard to extent and rapidity of improvement, patient satisfaction and any adverse events if any.

Introduction

Acne vulgaris is one of the most common dermatoses in the world. It is a chronic inflammatory disease of the pilosebaceous unit. Majority of the incidence of acne is seen in adolescence. Acne occurs over the seborrheic areas like face and trunk. It may manifest clinically as non inflammatory (open and closed comedones) or inflammatory (papules, pustules and nodules) lesions. The inflammatory process associated with acne may lead to post acne scarring and is common sequelae. Scarring occurs due to gain or loss of collagen with resultant formation of hypertrophic or atrophic scarring respectively. Scarring is a distressing phenomenon and is most unwelcome when it occurs on the face. Severe scarring on the face is physically disfiguring and causes significant psychological distress. The affected individual may suffer from lack of self confidence, low self-esteem and many other psychological ill effects. Even though post acne facial scarring is a challenging problem to manage there are various methods to improve the appearance of scar.

Epidemiology

Acne is an almost universal condition in younger people. Acne usually starts in the early teens near puberty with the onset of facial sebum production and facial comedones followed by inflammatory lesions. Acne lesions usually develop earlier in females as puberty occurs earlier in them. The major brunt of the disease is borne by the age group 16-20 years as shown by a study in India.[1] Mean age of onset was 15.97 years, affecting males more than females. Prevalence of acne in age group of 12-17 years is 50-60% in boys and 38-73% in girls by a study in India.[1] Scarring as a sequel to acne can occur in up to 95% of acne patients and 30% may develop cosmetically disfiguring scarring.[2]

Pathogenesis

Pathogenesis of Acne

Acne is a multifactorial disease. The four basic factors which have been identified include: (i) sebaceous gland hyperactivity and seborrhea (ii) abnormal follicular differentiation and

hyperkeratinization of the pilosebaceous duct, (iii) abnormal colonization of the pilosebaceous duct with microbial flora especially *P. acnes* and (iv) increased inflammation.

1. Sebaceous gland hyperactivity and seborrhea:

Increased production of sebum by sebaceous glands leads to development of acne.[18] Triglycerides and lipoperoxides in sebum have an active role in acne formation. Free fatty acids formed by the breakdown of triglycerides promote colonization of *P.acnes*, cause inflammation and is comedogenic.[19] Lipoperoxides produce proinflammatory cytokines and stimulate the peroxisome proliferator-activated receptor (PPAR) pathway, increasing sebum production.[20] Androgenic hormones such as testosterone and more active DHT also have a significant role in acne pathogenesis. These hormones act on the sebocytes and regulate their proliferation and differentiation.[21] Corticotropin releasing hormone also has a role and it is seen that corticotropin releasing hormone receptors are increased in the sebocytes of patients with acne.[22]

2. Comedogenesis :

Follicular epidermis including that of the infundibulum becomes hyperproliferative and the corneocytes become increasingly cohesive with the formation of a plug in the follicular ostium. The plug so formed further causes collection of keratin, sebum and bacteria in the follicle and dilation of the upper hair follicle producing a microcomedone.

Keratinocyte hyperproliferation is stimulated by DHT, subnormal levels of linoleic acid, increased interleukin 1 alpha (IL-1) activity and effects of *P.acnes*.[23, 24] Fibroblast growth factor receptor (FGFR)- 2 pathway also causes proliferation of corneocytes and is androgen dependent.[25]

Ductal hyperkeratinisation is seen histologically as microcomedones and clinically as blackheads, whiteheads and other forms of comedones such as macrocomedones .The number and size of follicular casts (micro-comedones) correlates with acne severity.[26]

3. Colonization of Intrafollicular duct with *P.acnes :*

P.acnes is a Gram-positive, anaerobic, and microaerobic bacterium found in the pilosebaceous follicle. Colonization of intrafollicular duct with *P.acnes* has significant role in comedogenesis and initiating inflammation. The breakdown of triglycerides into free fatty acids by *P.acnes*

further promotes its colonization resulting in comedogenesis .[19]The carbohydrate antigen present in the cell wall of *P.acnes* causes antibody development whose titres correlates with severity of acne.[27]

4. Inflammation:

The microcomedone formed by follicular plugging further expand by accumulation of keratin, sebum, and bacteria and eventually result in follicular wall rupture and extrusion of its material into the dermis. This will elicit inflammation with lymphocyte being the predominant cell type in the initial 24 hours followed by neutrophils.[28] It has been proved by various studies that inflammatory process starts even before comedo formation and is further increased by comedo formation.[29]

The antipropionobacterium antibody activates the complement system and initiates proinflammatory responses.[30] Elicitation of the delayed type hypersensitivity response and the production of lipases, proteases, hyaluronidases and chemotactic factors by *P.acnes* also promote inflammation.[31] Neutrophils release reactive oxygen species and lysosomal enzymes and adds to the severity of inflammation.[32] Moreover, *P.acnes* also binds to the toll-like receptor 2 (TLR2) on monocytes and neutrophils and stimulate the release of proinflammatory cytokines such as IL-1α, IL-8, IL-12, and TNF-α around the sebaceous follicle.[33, 34]

Pathogenesis of Acne Scarring

The uninhibited inflammatory process in acne leads to rupture of the follicular wall, marked perifollicular inflammation and abscess formation. All these events stimulate the wound healing process. Biological process involved in wound healing is a complex one and involves cellular components such as keratinocytes, fibroblasts, endothelial cells, nerve cells, inflammatory cells like lymphocytes, monocytes, and neutrophils, soluble chemical mediators, and extracellular matrix components. Three major events involved in the wound healing process are: (a) inflammation (b) formation of granulation tissue and (c) remodeling of matrix.[3]

a. Inflammation. Postacne erythema and hyperpigmentation develop as a result of following processes: initial blanching due to vasoconstriction, followed by vasodilatation and resultant erythema that stimulate melanogenesis. Inflammatory mediators released by granulocytes,

macrophages, neutrophils, lymphocytes, fibroblasts, and platelets initiate granulation tissue formation.[35] Histopathological study of acne scars by Holland et al. demonstrated a direct relationship between severity and duration of inflammation at the pilosebaceous unit and acne scarring. There by suggesting that treating early inflammation in acne may be the best approach to prevent scarring.[36]

b. Granulation Tissue Formation. Tissues that are damaged during the inflammatory process are repaired and new capillaries are formed. Neutrophils which are present during the initial stages are replaced by monocytes that eventually form macrophages and release various growth factors including platelet-derived growth factor, fibroblast growth factor, and transforming growth factors α and β. These chemical mediators stimulate the migration and proliferation of fibroblasts.[37] Fibroblasts produce collagen. The new skin formed is predominantly composed of type III collagen; and type I collagen occupies about one fifth of it. As the scar matures the proportion of collagen types changes and becomes similar to that of unwounded skin with 80% of collagen formed by type 1.[38]

c. Matrix Remodelling. Architecture of the extracellular matrix is maintained by the enzymes produced by the fibroblasts and keratinocytes. These enzymes, matrix metalloproteinases (MMPs) which degrade the extracellular matrix (ECM) and tissue inhibitors of MMPs (TIMP) act together and remodel ECM .[39]Any imbalance in the ratio of MMPs and TIMP can result in decreased or increased deposition of collagen and formation of an atrophic or hypertrophic scar respectively.[4]

Morphology and Classification

During the process of healing of active acne and matrix remodeling there can be a net loss or gain of collagen forming atrophic or hypertrophic scars. Atrophic scars associated with a loss of collagen are the major type of acne scar whereas hypertrophic scars and keloids form around only ten percent of acne scar.

Atrophic Scars[40]

Atrophic scars are further subclassified into ice pick, boxcar, and rolling scars.

Depending on the shape, 3 primary atrophic acne scars as described by Jacob et al:[5]

Icepick 60%–70% “V” shape

Rolling 15%–25% “M” shape

Boxcar 20%–30% “U” shape

This new classification system relates scar anatomy with the available effective treatment options, facilitating precise identity and classification of acne scar types

Icepickscars: Scars those are narrow (<2 mm), deep, sharply marginated epithelial tracts that extend vertically to the deep dermis or subcutaneous tissue are known as icepick scars. In this type of scars, the surface opening is typically wider than the deeper infundibulum (forming a ‘‘V” shape), and the scar tapers as it goes deeper (Fig 1).

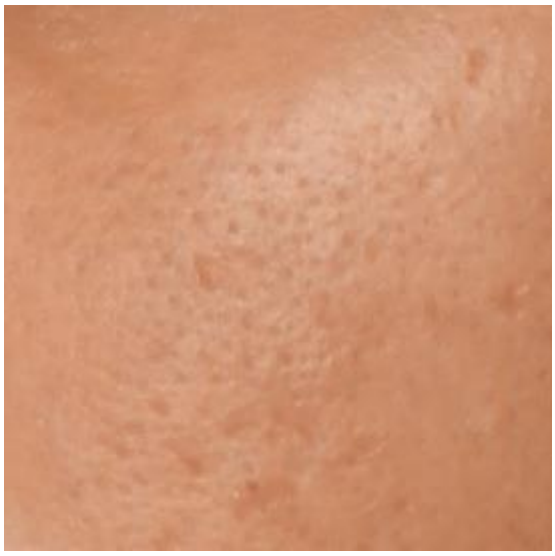

Figure 1: Icepick scars

Rolling scars: Scars forming as a result of dermal tethering of the dermis to the subcutis of otherwise relatively normal appearing skin characterizes rolling scars, and is usually wider than 4 to 5 mm. This abnormal fibrous anchoring leads to superficial shadowing and a rolling or undulating appearance to the overlying skin (‘‘M” shape) **(**Fig 2).

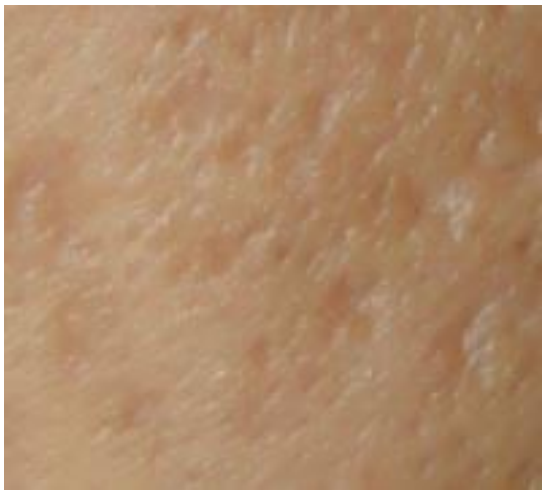

Figure 2: Rolling scars

Boxcar scars: Round or oval depressions with well defined vertical edges are known as boxcar scars. These scars do not taper towards the base and are wider at the surface than icepick scars. These scars are ‘‘U” shaped with a wide base. Boxcar scars may be shallow (0.1-0.5mm) or deep (≥ 0.5mm) and are most often 1.5 to 4 mm in diameter **(**Fig 3).

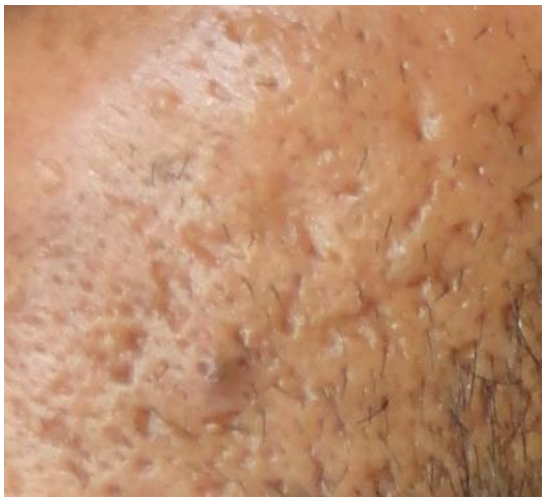

Figure 3: Boxcar scars

Hypertrophic and Keloidal Scars[40]

Increased collagen deposition and decreased collagenase activity during the process of healing in inflammatory acne results in either hypertrophic or keloidal scar. Pink, firm and elevated scars, that do not extend beyond the margins of the initial site of injury are hypertrophic scars and is

formed due to the deposition of bundles of thick hyalinized collagen within the borders of original injury . Hypertrophic scars have similar pathology to that of other dermal scars. Whereas scars that appear as reddish-purple papules and nodules which extend outside the borders of the original wound are keloids; and is formed due to the deposition of thick bundles of hyalinized acellular collagen in a whorled pattern. Darker-skinned individuals are more prone to develop hypertrophic and keloidal scars (Fig 4).

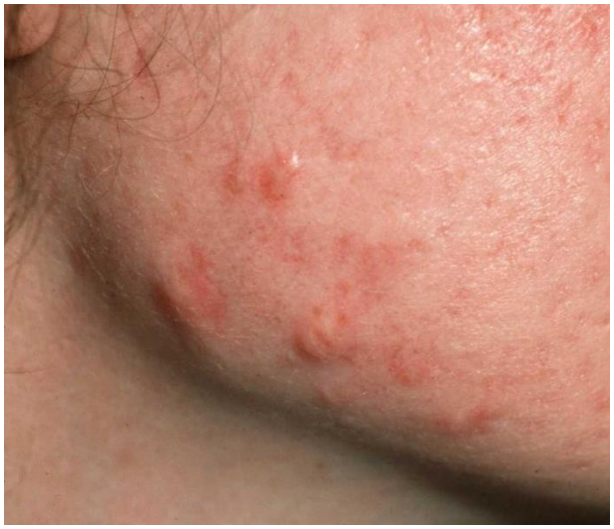

Figure 4: Keloidal scars

Grading of Acne Scars

Atrophic scars of various types can be present in the same individual and it becomes very challenging to identify them separately. To overcome this difficulty several classifications and scales have been proposed by other authors. The qualitative scale and the quantitative scale proposed by Goodman and Baron[6, 7] and the ECCA scale (Echelle d'Evaluation Clinique des Cicatrices d'Acné) by Dreno et al[41] are the most widely used scales.

The qualitative scarring grading system proposed by Goodman and Baron is simple and universally applicable and reproducible.[6] Depending on the severity, an acne scar is graded into four different grades according to this classification as shown in Table 1.

Table 1 --- Goodman and Baron Qualitative Scarring Grading System[6]

Grades of Post acne Scarring	Level of Disease	Clinical features
1	Macular	Erythematous, hyper/hypo pigmented flat marks. No contour changes.
2	Mild	Mild atrophy or hypertrophy scars that may not be obvious at social distances of 50 cm or greater and may be covered adequately by make up or the normal shadow of hairs.
3	Moderate	Moderate atrophic or hypertrophic scarring that is obvious at social distances of 50 cm or greater and is not covered adequately by make up or the normal shadow of hairs; but is still able to be flattened by manual stretching of the skin (if atrophic).
4	Severe	Severe atrophic or hypertrophic scarring that is evident at social distances greater than 50 cm and is not covered easily by make up or the normal shadow of the hairs; and is not able to be flattened by manual stretching of the skin.

Acne scars of milder types can be easily assigned a grade. But in severe post acne scarring, scars of different grades and severity may be present in the same individual making the task of assigning a qualitative grade according to Goodman and Baron a difficult one. Goodman and Baron has also proposed a quantitative global acne scarring assessment tool (Table 2) which takes into account not only the type of scars but also the number of each type of scar. [7]

Table 2 Goodmans Quantitative Global Acne Scarring Grading System[7]

Grade or Type	Number of Lesions 1 (1-10)	Number of Lesions 2 (11-20)	Number of Lesions 3(>20)
A) Milder scarring (1 point each) Macular erythematous pigmented Mildly atrophic, dish like	1	2	3
B) Moderate scarring (2 points each) Moderately atrophic, dish like Punched out with shallow bases small scars (<5mm)	2	4	6
C) Severe scarring (3 points each) Punched out with deep but normal bases, small scars (<5mm) Punched out with deep but abnormal bases, small scars (<5mm) Linear or troughed dermal scarring Deep, broad atrophic areas	3	6	9
D) Hyperplastic Papular scars Keloidal/Hypertrophic scars	2 (Area <5mm) 6	4 (Area 5-20 cm^2) 12	6 (Area >20 cm^2) 18

This allows more accurate assessment of acne scarring severity which can be reproduced with considerable accuracy and can be used for the evaluation of the efficacy of any therapeutic intervention. According to this system fewer points are assigned to macular and mild atrophic scars than to moderate and severe atrophic scars (macular or mildly atrophic: 1 point; moderately atrophic: 2 points; punched out or linear-troughed severe scars: 3 points; hyperplastic, papular scars: 4 points). The numerical value obtained on the basis of scar type is then multiplied by the multiplication factor based on the number of each type of lesion whereby, for 1-10 scars, the multiplier is 1; for 11–20 it is 2; for more than 20 it is 3.

The ECCA (Echelle d'Evaluation clinique des Cicatrices d'acné) for facial acne scarring is also a quantitative scale. This grading system takes into consideration the type and number of individual scar. Each scar type is assigned a weighing factor depending on the disfigurement that it causes and scar types that are more disfiguring are given a higher weighing factor. Specific scar types and their associated weighting factors are the following: atrophic scars with diameter less than 2 mm: 15; U-shaped atrophic scars with a diameter of 2–4 mm: 20; M-shaped atrophic scars with diameter greater than 4 mm: 25; superficial elastolysis: 30; hypertrophic scars with a less than 2-year duration: 40; hypertrophic scars of greater than 2-year duration: 50. A semiquantitative assessment of the number of each of these scar types was then determined with a four-point scale, in which 0 indicates no scars, 1 indicates less than five scars, 2 indicates between five and 20 scars, and 3 indicates more than 20 scars.. The total score can vary from 0 to 540. The relative severity of scarring caused by each scar type can be estimated by this method. In recent studies on the reliability of this scale, seven dermatologists underwent a 30-min training session prior to the evaluation of ten acne patients. There was no statistical difference in score grading between participating dermatologists. The global scores, however, varied from a minimum of 15 to a maximum of 145. Unfortunately, a statistical estimate of reliability within and between raters was not provided. The potential advantages of this system include independent accounting of specific scar types, thereby providing for separate atrophic and hypertrophic subscores in addition to total scores. Potential shortcomings include restriction to facial involvement, time intensity, and undetermined clinical relevance of score ranges.[41]

Treatment[42-54]

Acne scarring is permanent; however, the appearance can be improved with various medical, laser, and surgical approaches.

Treatment of acne scars can be broadly classified as:

1. Medical Management
2. Surgical and Procedural Management
3. Tissue augmentation
4. Light , laser and energy Therapy

Medical Management: It includes retinoids, topical/intralesional steroids, silicone dressing, and various other topical and injectable substances. Hypertrophic scars, keloids, and pigmentary changes are the usual focus of medical management.

Surgical Management:

1) Punch Excision
2) Elliptical excision
3) Punch Elevation
4) Skin graft
5) Subcision
6) Debulking

Procedural Management

1) Cryosurgery
2) Electrodessication
3) Radiation treatment
4) Chemical peels
5) Microdermabrasion
6) Dermabrasion
7) Microneedling

Tissue Augmentation: Scars may be filled with collagen injections, artificial dermal fillers, or autologous fat transfer.

For Atrophic scars:[40] Chemical peels, dermabrasion/microdermabrasion, laser treatment like Carbon dioxide laser, Erbium YAG laser, NdYAG, Diode lasers, punch techniques, subcision, dermal grafting, tissue augmentation agents such as fat transplantation, hyaluronic acid, skin needling, combined therapy.

For Hypertrophic scars:[40] Silicone gel, cryotherapy, intralesional steroid therapy, pulsed dye laser, surgery. Other treatment options for hypertrophic acne scars and keloids that can be taken into account includes elastic compression, intralesional injection of 5-fluorouracil, imiquimod, interferon, radiotherapy, and bleomycin.

Some of these methods like lasers are very costly and out of reach of an average patient while others are either invasive or not so efficacious. So there is always a need for development of relatively affordable, efficacious and less invasive methods.

Topical Retinoids and Tazarotene

Topical retinoids is a mainstay of acne treatment because it is effective against both acne and post acne scarring. The broad anti-acne activity and safety profile of topical retinoid justifies their use as first-line treatment in most types of non-inflammatory and inflammatory acne.[55] Retinoids are synthetic derivatives of retinol (vitamin A). Tretinoin (all-trans retinoic acid), isotretinoin (13-cis retinoic acid), adapalene (derived from naphthoic acid) and tazarotene (acetylenic retinoid) are the retinoids that are used in the topical preparation.[56] The tazarotene is a new third generation topical acetylenic retinoid. Tazarotene was approved by the US-FDAin June 1997 for acne vulgaris .[57]Topical tazarotene is therapeutically effective as 0.1% gel or 0.1% cream.[10, 11]Tazarotene (0.1%) was found to be superior to adapalene (0.1% gel) and tretinoin (0.025%, 0.1%) for the treatment of acne vulgaris.[12]

In 1975, tretinoin along with hydroquinone and dexamethasone was first reported to have efficacy in reducing PIH.[58] In further studies, tretinoin was used as monotherapy and in combination with hydroquinone and either lactic acid or glycolic acid.[59-61] More recently, adapalene monotherapy was also reported to be effective, though only in a trial without a placebo comparison group. [62] Tazarotene previously has shown efficacy in reducing PIH associated with pseudofolliculitis barbae, as well as in reducing hyperpigmentation associated with photodamage, epidermal nevi, and acanthosis nigricans.[17, 63] Because tazarotene also is a well-established treatment for acne vulgaris, and has shown antiacne efficacy without the induction of PIH in patients from darker racial ethnic groups, tazarotene is a logical choice to investigate for the treatment of PIH in darker-skinned patient.[10] In studies on photodamaged skin, tazarotene has been shown to be effective in the reduction of mottled hyperpigmentation and fine wrinkling,

with significant improvements noted more rapidly for mottled hyperpigmentation (week 12) than fine wrinkling (week 24).[17, 63]Intreating PIH with tretinoin monotherapy, a significant advantage of tretinoin over vehicle was first reported at week 12.[59] Thus, it is possible that tazarotene may act slightly more rapidly than tretinoin.

Mode of Action of Topical Retinoids and Tazarotene

Retinoids act by binding to the nuclear hormone receptors retinoic acid receptors (RARs) and retinoid X receptors (RXRs) and cytosolic binding proteins receptor family and causes transcription of retinoic acid-responsive genes.[64] There are three subtypes (α, β, γ) in each receptor family and they form homo and heterodimers and then bind to a DNA stretch called a 'responsive element' (RARE and RXRE) and induce the expression or downregulation of target genes in a ligand-dependent manner. RARγ and RXRα are the most common subtypes of retinoid receptors in human skin.[65, 66]Tazarotene is selective for the beta and gamma subtypes of retinoic acid receptors.

Retinoids reduce hyperpigmentation of the skin by reducing epidermal melanin by inhibition of tyrosinase and tyrosinase-related protein 1(TRP-1) activity, reduction of melanosome transfer from melanocytes to keratinocytes and increasing the turnover of melanin –laden keratinocytes.

Biologic effects

Retinoids normalize keratinocyte differentiation and reduces proliferation thereby increasing follicular epithelial turnover and the shedding of corneocytes.[8] As a result mature comedones are expelled and further formation of microcomedone is suppressed.[67] This prevention of hypercornification of pilosebaceous follicle decreases the colonization by *P.acne*. The expression of the transcription factors, such as AP-1, are also regulated by retinoids .[68]In effect, the genetic expression of growth factors such as vascular endothelial growth factor and degradative enzymes such as matrix metalloproteases which are involved in inflammatory responses are modified. It also reduces the expression of inflammatory markers. Furthermore, collagen synthesis is stimulated and oxidative stress is prevented by retinoids and thereby exerts an anti-aging effect.[9, 56] Various studies have also demonstrated a direct immunomodulatory activity for topical retinoids.[69, 70]

Safety and Tolerability

Tazarotene has a low potential for systemic adverse effects following topical application as only less than 6% of the applied drug is absorbed into plasma.[71] It is then rapidly metabolized into hydrophilic metabolites such as tazarotenic acid which are eliminated from the blood in the urine and feces.[72] There is no systemic accumulation of the drug. Once-daily application leads to better patient compliance. The selectivity of tazarotene for the beta and gamma subtypes of retinoic acid receptors minimizes the risk of adverse effects.Local adverse effects of tazarotene are similar to those observed with other topical retinoids and include erythema, burning/stinging, itching, and dryness.[55] The irritative potential of tazarotene can be reduced by short-contact therapy once or twice daily or by use of an every other day regimen.[73]It can also be used as short contact therapy where application, after an initial contact period of 2 minutes, is increased in 1-minute increments, at intervals of at least 3 days, to a maximum of 5 minutes. The contact period is reduced to 30 seconds if there is peeling, erythema, dryness, burning, or itching; the contact period is then increased in 30-second intervals every 3 days, if tolerated, to a maximum of 5 minutes.[73]The cream is generally better tolerated than the gel.[74] The severity of skin irritation caused by tazarotene is usually mild and improves with time.[12]

Tazarotene is designated pregnancy category X, prohibiting its use during pregnancy and breastfeeding. Women of reproductive age group should use adequate birth-control measures when topical tazarotene is being used. Teratogenicity was reported in animals after oral administration of high doses of tazarotene but not after topical use.[75]

Microneedling

Microneedling with dermaroller is a novel, minimally invasive therapeutic method for the management of scars, particularly acne scars.[13] Percutaneous collagen deposition by “Scar needling” using subcision was first developed by Orentreich and Orentreich in 1995.[42]

Figure 5: Dermaroller device

Dermaroller as a method of percutaneous collagen induction was described by Fernandez in 2006.[14] The principle behind the technique is that the damaged collagen bundles in the upper layer of the dermis that causes scars are broken down by puncturing the skin with small needles multiple times resulting in the formation of new collagen immediately beneath the epidermis.[15, 42]192 fine microneedles arranged in eight rows on a drum shaped roller is the standard dermaroller used for acne scars (Fig 5). The diameter of the microneedle is 0.1 mm and the length may vary (0.5–2.5 mm).[16]When the scarred skin is rolled with dermaroller multiple times in various directions, micro wounds are formed in the papillary dermis. Rolling with these microneedles, in various directions, lead to microtrauma to the superficial dermis without damaging the epidermis except for the minute holes which heal rapidly. The tiny wounds so formed in the superficial dermis cause the release of growth factors and stimulation of the formation of new collagen.[15, 76]Penetration of microneedle into the skin causes localized damage and rupture of fine blood vessels with minor bleeding .[13] Hundreds of such tiny wounds placed close to each other trigger the process of normal wound healing and was shown by different studies.[2, 15, 76] The process of normal wound healing progress through three consecutive stages of inflammation, proliferation and tissue remodeling.

Stage1: Inflammation stage. Immediately after the injury chemotactic factors are released by platelets and causes further invasion of platelets, neutrophils, and fibroblasts at the site of injury.

Stage2: Proliferation stage. The neutrophils which are present in the initial stage are replaced by monocytes which later change into macrophages. These macrophages release various growth factors like platelet-derived growth factor, fibroblast growth factor, and transforming growth factors alpha and beta. The migration and proliferation of fibroblasts occur in response to this stimulation. Keratinocytes increase the production of laminin and collagen types IV and VII which in turn result in reestablishment of the basement membrane.

Stage3: Remodeling stage. The major component involved in this stage is fibroblasts which form collagen in the upper dermis. The whole stage may continue for months after the injury or may even extent over a period of a year or longer.[15, 77]

In the initial phases of wound healing the main type of collagen formed is collagen III. During the tissue remodeling stage it is gradually replaced by collagen I. The gradual conversion of collagen III into collagen I over a period of a year or more is brought by collagenases and matrix proteinases ,which remains in the area for 5 to 7 years.[78] This whole process of tissue damage, inflammation and remodelling is known as PCI (percutaneous collagen induction).[15, 76] The effect of microneedling has also been explained on the basis of a demarcation current produced among cells when microneedles penetrate the skin, which triggers a cascade of production of growth factors that stimulate the healing phase.[15, 76] To get optimal results with dermaroller multiple sittings are generally required with a time interval that varies from 4 to 8 weeks.[16] A minimum of six weeks is recommended between two treatments as it takes that long for new natural collagen to form. Three to four treatments may be needed for moderate acne scars .[13]In different studies, total numbers of treatment session performed varied from 2 to 6. It is not established yet if more number of sittings could result in still higher efficacy.[16] Apart from acne scars the technique of microneedling is also used in the management of stretch marks, wrinkles, photoageing, pigmentary disorders, burn-related scars, and big pores. [13, 79]It is a simple and relatively cheap modality that also can be used for transdermal drug delivery. Microneedling is done as a simple office-based procedure. As the microholes formed during the procedure close immediately, postoperative infections do not occur.[13] The side effects and the downtime are minimal following the procedure because the enhancement of dermal ECM proteins occurs without ablation of the epidermis in contrast to the ablative lasers.[80, 81] Thus after dermaroller treatment, skinbarrier function remains undisturbed and this hastens recovery and limits the risk

of scarring.[82] Eventhough much of the epidermis remain intact in other modalities, such as nonablative and fractional lasers, these can cause thermal activation of melanocytes and dyspigmentation in patients with darker phototypes .Other lasers can also use wavelengths that are absorbed by melanin. In contrast, microneedling does not target specific chromophores in the skin or using thermal energy, and therefore has minimal effect on pigmentation.[78, 83, 84]The procedure is well tolerated and well accepted by the patients, is cost-effective, can be done on all skin types and on areas not suitable for peeling or laser resurfacing, such as near eyes. Microneedling with dermaroller can be combined with other acne scar treatments like subcision, chemical peels, microdermabrasion, and fractional resurfacing, thus maximizing the benefits to the patients.[13]

Side effects that have been reported in a study by Dogra et al[16] include procedural pain, transcient post procedure erythema, bruising and swelling, PIH and tram-track scarring. Most of these were mild in nature. PIH was mainly due to inadequate sun protection. Tram-track patterned scarring was seen as a worst side effect and was thought to be due to larger needling device or strong pressure exerted while doing the procedure. Photoprotection is the only post procedure care demanded by the technique.[13]

There are various studies comparing the efficacy of microneedling with other modalities for atrophic post-acne scarring (Table 3). In these studies microneedling was used either alone or in combination with other modalities to compare the outcome. The outcome of these studies established microneedling as a successful procedural method for atrophic post-acne scarring. There is no study on efficacy of topical tazarotene in atrophic post-acne scar to the best of our knowledge. Our present study is aimed at head to head comparison of topical tazarotene and microneedling in the improvement of atrophic post-acne scars. If topical tazarotene is proved to be as effective as microneedling in atrophic post-acne scars, it may change the current management strategy of atrophic post-acne scarring which is mainly physician dependant.

Author (Year)	No. of patients	Study design (final assessment)	Treatment sessions (interval)	Scoring method	Outcome	Comments
Majid[85] (2009)	36	PCI (2 months after last session)	4 sessions or satisfactory outcome whichever is earlier (4 weeks)	Goodman and Baron Qualitative scale 1-10 point scale (subjective)	72.2% improved by 2 grades, 16.7% improved by 1 grade.	Scars other than post acne scars (5 patients)included in study
Fabbrocini et al.[15] (2009)	32	PCI (8 weeks after last session)	2 (8 weeks)	Goodman and Baron Qualitative scale 10 point scale	Significant reduction in severity grade of acne scars	
Laheta et al.[76] (2011)	30	Group 1- PCI Group 2- 100% TCA cross (4 weeks after the last session)	4 (4 weeks)	Weighted scale followed by a quartile grading scale	Mean improvement Group 1- 68.3% Group 2- 75.3%	
Sharad[86] (2011)	30	Group A- PCI alone Group B- PCI + 35% GA peel (3 months after the last session)	Group A- 5 (6 weeks) Group B- 5 sessions of each alternatively (3 weeks)	ECCA grading	Mean improvement Group A- 31.33% Group B- 62%	
Leheta et al.[87] (2012)	24	Group 1 : deep peeling using phenol Group 2: PCI combined with TCA 20% (8 months from starting	Group 1-1 Group 2-4 (6 weeks)	Weighted scale followed by a quartile grading scale	75.12% and 69.43% improvement in scar in group 1and 2 respectively	Blinded evaluation

		the treatment)				
Lehetaet al.[88] (2012)	39	Group 1 - PCI +20% TCA Group 2 – 1540 nm nonablative fractional laser Group 3 - alternating treatment with above two modalities. (12 months from starting the treatment)	In all the groups 6 sessions (4 weeks)	Weighted scale Followed by a quartile grading scale	59.79%, 61.83%, 78.27% improvement in Group 1, 2, 3 respectively.	Blinded evaluation
Chawla[89] (2014)	30	Split face study PCI + PRP on right side PCI +vitamin C on left side of the face (after the last session)	4 (1 month)	Goodman and Baron Qualitative scale	Reduction in scarring by two grades seen in 18.5% patients with PRP as compared to 7% patients who received treatment with vitamin C. Up gradation by one score similar in both cases.	
Dogra et al.[16] (2014)	36	PCI (1 month after last session)	5 (4 weeks)	Photograph assessment on a quartile scale	Mean 50%-75% improvement in the majority of subjects	

Asif et al.[90] (2015)	50	Split face study- PCI + Intradermal injections and topical application of PRP on right half; PCI + intradermal administration of distilled water on left half (1 month after last session)	3 (1month)	Goodman and Baron Qualitative scale Goodman's Quantitative scale	Right and left halves showed 62.20% and 45.84% improvement, respectively, on Goodman's Quantitative scale. 40% improved by 2 grades and 60% improved by 1 grade over right half vs 10% and 84% respectively over left half on Goodman's Qualitative scale	Blinded evaluation

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512 **Table 1. Review of literature on microneedling in atrophic acne scar.**

513 ECCA= Echelled'Evaluationclinique des Cicatrices d'acne′; PCI=Per-cutaneous collagen
514 induction; PRP=Platelet rich plasma; TCA=Trichloro acetic acid; GA=Glycolic acid

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AIMS AND OBJECTIVES

Primary objective:

To compare the efficacy of microneedling versus topical 0.1 % tazarotene gel in the management of moderate to severe atrophic acne scars.

Secondary objective:

To evaluate the tolerability and adverse effects of the two treatment options.

MATERIALS AND METHODS

Design: Prospective, single blinded, randomized, pilot study.

Methodology:

Patients with atrophic acne scars attending Dermatosurgery Clinic of Department of Dermatology, Venereology and Leprology; Postgraduate Institute of Medical Education and Research, Chandigarh, India will be screened for the study. A total of 36 subjects of atrophic post acne scars who are satisfying inclusion and exclusion criteria will be recruited.

Inclusion Criteria:

- Patients with grade 2 to grade 4 atrophic acne scars, classified on the basis of Goodman's Qualitative classification.[6]
- Should not have undergone any surgical and/or laser treatment for acne scars in the past 1 year.

Exclusion Criteria:

- Active acne
- History of keloidal tendency/hypertrophic or keloidal scarring on the face due to acne
- Facial scars due to reasons other than acne like varicella, trauma, burns etc
- Collagen vascular disease, bleeding disorders
- Any active bacterial , fungal or viral infection over face
- Pregnant and lactating females
- Known hypersensitivity to tazarotene
- Age less than 18 years
- Patients on anticoagulant therapy or aspirin

In this split-face design, the face of each patient will be randomized for microneedling on one side and topical tazarotene 0.1 % gel on opposite side. Randomisation will be done using computer generated random number table. Follow ups will be done at every month until treatment completion (3 months) and 3 months after last treatment session. Patient assessment will be done using subjective and objective methods. Study design is depicted in Figure6.

Primary outcome:

- Change in acne scar severity grade from baseline at 3 months, and at 6months.

Secondary outcomes:

- Patient satisfaction using *Patient's global assessment score*.
- Adverse events if any.

Study design

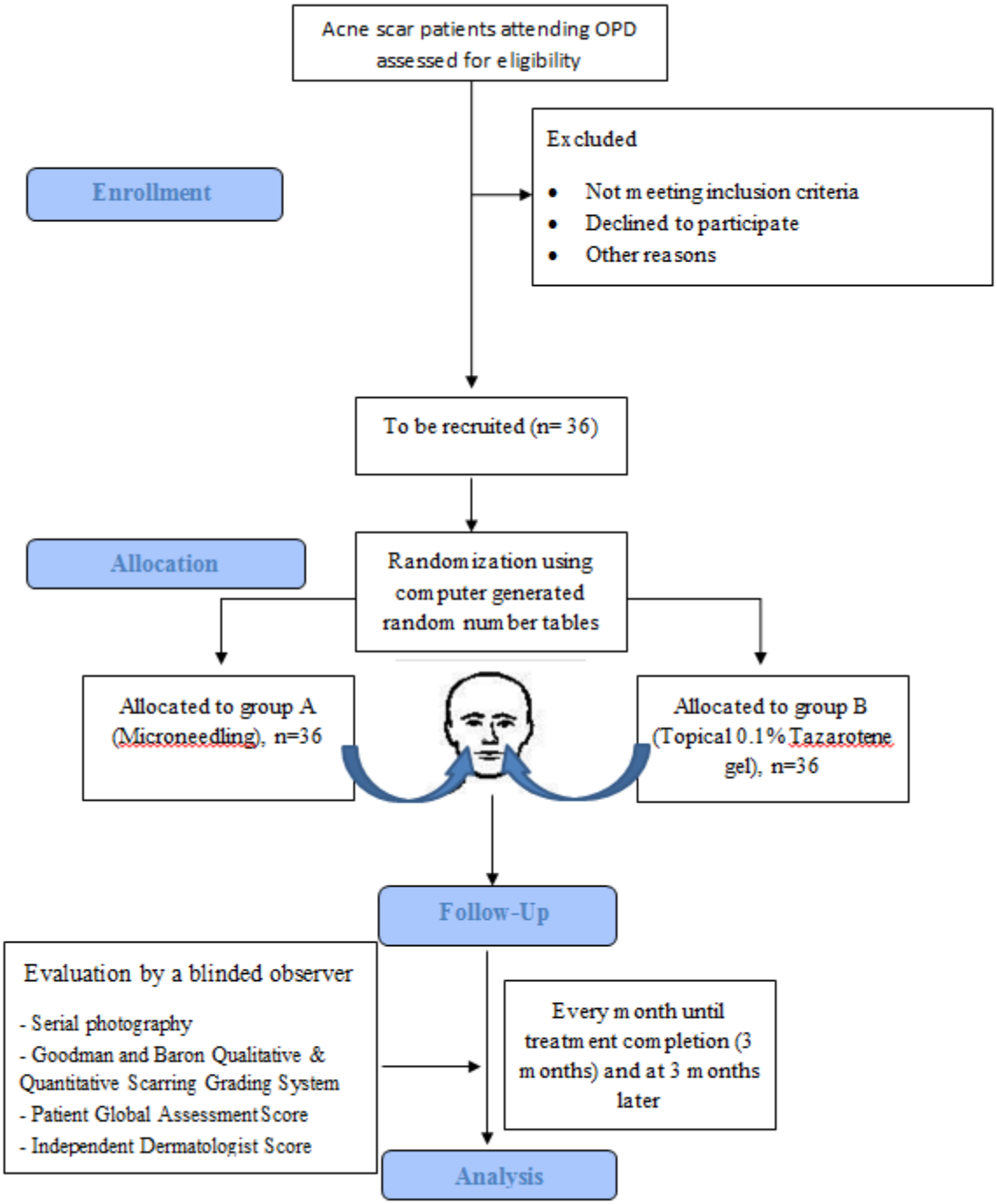

Figure 6: Study design

Patient Assessment

A detailed history, including onset, course, and duration of scars, previous acne and acne scar treatments, and post-treatment complications such as hyperpigmentation or keloid formation will be taken. Subjects will be then recruited based on inclusion/exclusion criteria.

At the first visit, a pro forma will be filled noting the baseline characteristics, history and examination findings. Dermatologic examination to assess the skin type, the scar type (ice pick, boxcar, and rolling type), the scar severity according to the Goodman and Baron qualitative and quantitative acne scarring grading system (Table 1 and 2) will be performed for every patient. Complete hemogram, renal function tests, liver function tests, prothrombin time, partial thromboplastin time and urine pregnancy test (in female patients) will be performed for every patient. Baseline photography will be performed in the same settings with respect to patient positioning, background, lighting and camera settings for every patient.

Possible side effects of each procedure such as erythema, edema, exfoliation, pain and hyperpigmentation will also be explained. Then, informed consent will be taken for the procedure from every patient.

Table 1 --- Goodman and Baron Qualitative Scarring Grading System[6]

Grades of Post acne Scarring	Level of Disease	Clinical features
1	Macular	Erythematous, hyper/hypo pigmented flat marks. No contour changes.
2	Mild	Mild atrophy or hypertrophy scars that may not be obvious at social distances of 50 cm or greater and may be covered adequately by make up or the normal shadow of hairs.
3	Moderate	Moderate atrophic or hypertrophic scarring that is obvious at social distances of 50 cm or greater and is not covered adequately by make up or the normal shadow of hairs; but is still able to be flattened by manual stretching of the skin (if

		atrophic).
4	Severe	Severe atrophic or hypertrophic scarring that is evident at social distances greater than 50 cm and is not covered easily by make up or the normal shadow of the hairs; and is not able to be flattened by manual stretching of the skin.

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584 **Table 2 Goodmans Quantitative Global Acne Scarring Grading System[7]**

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Grade or Type	**Number of Lesions 1 (1-10)**	**Number of Lesions 2 (11-20)**	**Number of Lesions 3(>20)**
A) Milder scarring (1 point each) Macular erythematous pigmented Mildly atrophic, dish like	1	2	3
B) Moderate scarring (2 points each) Moderately atrophic, dish like Punched out with shallow bases small scars (<5mm)	2	4	6
C) Severe scarring (3 points each) Punched out with deep but normal bases, small scars (<5mm) Punched out with deep but abnormal bases, small scars (<5mm) Linear or troughed dermal scarring Deep, broad atrophic areas	3	6	9
D) Hyperplastic Papular scars Keloidal/Hypertrophic scars	2 (Area <5mm) 6	4 (Area 5-20 cm^2) 12	6 (Area >20 cm^2) 18

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Treatment protocol:

After patient selection, the face of each subject will be randomized to receive microneedling on one side (group A) and topical tazarotene gel on opposite side (group B). In this study design; subject's face is arbitrarily divided into two equal halves by drawing arbitrary line touching glabella and mid chin through tip of nose. Randomisation will be done using computer generated random number tables. One set of eighteen random numbers ranging from 1 – 36 are generated in sequence. Those patients falling in this random number sequence will get microneedling on right side of face and tazarotene 0.1% gel treatment on left side of face, while others will get treatment vice versa.

Group A: The treatment protocol in the group A will consist of four sessions of microneedling at monthly intervals. (0, 1, 2, 3 months)

Group B: The treatment protocol in the group B will consist of night time application of Tazarotene 0.1% gel during the entire study period. (3 months)

Microneedling:

Microneedling treatment will be performed with a standard dermaroller by the same investigator, for a total of four sittings at monthly intervals. Prior to the procedure, thick layer of topical anesthetic mixture (lignocaine and prilocaine) under occlusion will be applied over face and left for 1 hour. Dermaroller with 1.5 mm needle length will be used.Patients will be placed in supine position with head stable and rolling will be performed eight times in four different directions, perpendicular and diagonal to each other with to-and-fro motion. The end point will be uniform pinpoint bleeding. Uniform and firm pressure will be applied to the roller, and the performing physician will remain the same throughout the study. After treatment, the area is wetted with saline pads.The face will be cleaned with distilled water after 1 hour and any bruise or other adverse effects will be noted if any. The subjects will be instructed to follow strict photo protective measures including application of broad spectrum sunscreen (SPF 30).

Topical Tazarotene 0.1% gel

Patients will be instructed to apply 0.1% tazarotene gel as a thin film over the affected area once daily in the evening. . They will be instructed to apply tazarotene 0.1% gel approximately 15 to

20 minutes after washing their face in the evening by placing a pea-sized amount in the palm of their hand and, using the tip of a finger to cover the entire half of face. Patients who experience facial dryness will be allowed to use a moisturizing cream during the day (entire face), but the use of any other lotions, creams, medicated powders, or solutions on the face will be prohibited. They will also be instructed to follow strict photo protective measures including application of broad spectrum sunscreen of SPF 30.

Follow-up

All the patients will be followed up at monthly intervals for three months and then at 6^{th} month from baseline. Digital photography will be done at 3^{rd} and 6^{th} month follow up visits. Any adverse effect experienced by the patient will be noted separately on each side of the face at each follow-up visits. In addition, the tolerability of the medication will be evaluated for erythema, burning, peeling, and dryness.

Goodman's qualitative and quantitative acne scarring grading system scoring will be performed at 3^{rd} and 6^{th} month follow up visits. Patients will be also assessed by an independent dermatologist (TN/SD) for clinical improvement and scored on a scale of 0 (no improvement) to 10 (maximum) at 3^{rd} and 6^{th} month follow up visits. All patients will be instructed to assess themselves using Patients' Global Assessment Score 0 (no response) to 10 (maximum) at 3^{rd} and 6^{th} month follow up visits. If required, previous self-scores will also be shown to each patient and thus allowing assessment of the degree of improvement to make further changes in the scores.Hence, both objective and subjective evaluation of the results shall be done. Pre- and post-treatment Goodman's Qualitative and Quantitative scores, independent dermatologist score, and patient satisfaction scores will be timely updated on an excel sheet for each patient.

Pre- and post-treatment Goodman's Qualitative and Quantitative score

The scars will be graded using grading system as used in the beginning (Goodman and Baron qualitative and quantitative acne scarring grading system) at 3^{rd} and 6^{th} month follow up visits. The improvement will be rated as poor, good and excellent depending upon the change in grade of acne scars. An improvement by two grades will be considered as excellent, one grade will be rated as good and no up gradation will be labelled as poor response.

Patients' Global Asesssment Score

Final patient satisfaction scores will be calculated for right and left halves of face of each patient. Score 0 was taken as unsatisfied, 1–3 slightly satisfied, 4–5 satisfied, 6–7 fairly satisfied, and 8–10 highly satisfied.

Photographic evaluation

The patients will be photographed using a 16.1 mega pixcels digital camera at the baseline and at 3rd and 6th month follow up visits. Digital photographs of both sides of the face will be taken under consistent background, position and lighting and compared with the pre-treatment images. Photographs will be captured at a distance of 50 and 10 cm of both halves of the face. Later, these photographs will be assessed by an independent dermatologist (TN/SD) for the final evaluation of acne scars.

Independent dermatologist score

Final independent dermatologist scores will be calculated for right and left halves of face of each patient. Score 0 was taken as no response, 1–3 poor response, 4–5 fair response, 6–7 good response and 8–10 excellent response.

STATISTICAL ANALYSIS

Sample size was estimated based on previous studies on microneedling. Our sample size came out to be 32 patients at a power of 80% & confidence interval of 95%. For possible dropouts, it was decided to include 36 patients.

The statistical analysis will be carried out using Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, version 22.0 for Windows). Discrete categorical data will be presented as n (%); Continuous data will be written as either in the form of its mean and standard deviation or in the form of its median and interquartile range, as per the requirement. The Normality of quantitative data will be checked by measures of Kolmogorov-Smirnov tests of Normality. For time related variables of scores or for comparison of two sides of scores, Wilcoxon Signed rank test will be applied; for normally distributed data ANOVA followed by Post Hoc Multiple Comparisons test (Dunnet t-test) will be carried out. Categorical data comparisons will be made by Pearson Chi-square test or Fisher's exact test as appropriate. All the statistical tests will be two-sided and will be performed at a significance level of α=.05.

ETHICAL JUSTIFICATION

This planned study is to be undertaken in patients of atrophic post acne scars. Microneedling is one of the common surgical procedures performed in day care setting for the improvement of acne scars with minimal side effects, if any. Topical tazarotene has been used in the treatment of acne and post acne scars. Both the procedures are to be carried out in the day care settings, without any in-patient hospital stay. These treatment modalities are affordable to most of the patients and do not impart much financial burden. By this study our aim is to establish topical tazarotene 0.1% gel as an effective method in the treatment of atrophic post acne scars using microneedling as a control. This in the long run will be helpful to the patients in terms of cost-effectiveness and ultimately the outcome.

Informed consent will be obtained from each patient prior to recruitment in the study. Patients will be explained regarding the study and the two treatment modalities used. To detect any adverse effect at the earliest, periodic visits of the patient are planned at regular intervals and will be managed accordingly. All necessary steps would be undertaken to ensure safety and convenience to the patients during entire study period.

Confidentiality of the study subjects will be maintained. No element of compulsion will be exerted. Moreover, the patients who may deny participating, would be excluded from study without asking for any reason thereof.

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ANNEXURE I

CONSENT FORM

Department of Dermatology, Venereology and Leprology

Postgraduate Institute of Medical Education and Research, Chandigarh 160012 (India)

Microneedling versus topical Tazarotene 0.1% gel for the treatment of atrophic post acne scars - a randomized controlled study

Name of the participant: _____

Name of the Investigator: Dr.Afra TP

Name of the Institution: PGIMER, Chandigarh

I, age CR. No exercising my free power of choice, hereby give my consent to be included as a subject in the study titled "Microneedling versus topical Tazarotene 0.1 % gel for the treatment of atrophic post acne scars- a randomized contolled study."

- I have been explained in a language understandable to me, the nature of the treatment, its expected benefits and possible side effects and I am willing to undergo any necessary investigations.
- I have been informed that for academic and scientific purposes, my face will be photographed before, during and after the study.
- I will allow the use of my photographs for presentation and publication purposes with the understanding that I will never be identified by name.
- I hereby give permission to the investigators to release the information obtained from me, as a result of participation in this study, to the sponsors, regulatory authorities, government agencies, and ethics committee. I understand that they may inspect my original records.
- I am aware that I will have to come to PGIMER, Chandigarh for follow up at least 4 times over a period of 6 months for the proper conduct of study.
- I am also aware of my right to opt out of the study any time during the course trial without having to give the reason for doing so.
- My signature on this form indicates that I:
  - Have carefully read and understood the information provided in this form
  - Have been explained the nature of this study and give my consent for inclusion in the study.

Name and signature of patient Name and signature of investigator

Date Name and signature of witness

968 **ANNEXURE II**

969 **STUDY PROFORMA**

970 **Microneedling versus topical Tazarotene 0.1 % gel for the treatment of**
971 **atrophic post acne scars - a randomized controlled study**

972 **Department of Dermatology, PGIMER, Chandigarh**

973 **Name…… Age/Sex…… CR No……**
974 **Dermatosurgery Clinic No…… Mob No……..**

975

976 **Chief complaints:**

977

978 **Total duration:**
979 **Previous treatment for acne and acne scar:**
980 **H/o post treatment complication:**
981 **Fitzpatrick skin type:**
982 **Predominant scar type:**
983

	0 week	1st month	2nd month	3rd month	6th month
Goodman's quantitative score					
Goodman's qualitative score					
Patient's global assessment score					
Independent dermatologist score					
Adverse effect					

984

Investigations	
Hb	
Total count	
Differential Count	N L E M B
Platelets	
RFT	
LFT	
PT/APTT	

Goodman and Baron Qualitative Scarring Grading System[6]

Grades of Post acne Scarring	**Level of Disease**	**Clinical features**
1	Macular	Erythematous, hyper/hypo pigmented flat marks. No contour changes.
2	Mild	Mild atrophy or hypertrophy scars that may not be obvious at social distances of 50 cm or greater and may be covered adequately by make up or the normal shadow of hairs.
3	Moderate	Moderate atrophic or hypertrophic scarring that is obvious at social distances of 50 cm or greater and is not covered adequately by make up or the normal shadow of hairs; but is still able to be flattened by manual stretching of the skin (if atrophic).
4	Severe	Severe atrophic or hypertrophic scarring that is evident at social distances greater than 50 cm and is not covered easily by make up or the normal shadow of the hairs; and is not able to be flattened by manual stretching of the skin.

Goodmans Quantitative Global Acne Scarring Grading System[7]

Grade or Type	Number of Lesions 1 (1-10)	Number of Lesions 2 (11-20)	Number of Lesions 3(>20)
A) Milder scarring (1 point each) Macular erythematous pigmented Mildly atrophic, dish like	1	2	3
B) Moderate scarring (2 points each) Moderately atrophic, dish like Punched out with shallow bases small scars (<5mm)	2	4	6
C) Severe scarring (3 points each) Punched out with deep but normal bases, small scars (<5mm) Punched out with deep but abnormal bases, small scars (<5mm) Linear or troughed dermal scarring Deep, broad atrophic areas	3	6	9
D) Hyperplastic Papular scars Keloidal/Hypertrophic scars	2 (Area <5mm) 6	4 (Area 5-20 cm^2) 12	6 (Area >20 cm^2) 18

ANNEXURE III

PATIENT INFORMATION SHEET

SPONSOR: MD Thesis work.

INVESTIGATOR: Dr Afra T P

GUIDE: Dr Tarun Narang

Co-GUIDE: Dr Sunil Dogra

Name of Participant:

Title: Microneedling versus topical Tazarotene 0.1 % gel for the treatment of atrophic post acne scars - a randomized controlled study

You are invited to take part in this research study. The information in this document is meant to help you decide whether or not to take part. Please feel free to ask if you have any queries or concerns.

You are being asked to participate in this study being conducted in PGIMER Chandigarh because you satisfy our eligibility criteria which are:

- Patients with grade 2 to grade 4atrophic acne scars, classified on the basis of Goodman's Qualitative classification
- Should not have undergone any surgical and/or laser treatment for acne scars in the past 1 year.

And with no contraindication for the treatment methods to be used in the study, which means absence of any disease or condition likely to get worsened by the methods under study, which are

- Active acne
- History of keloidal tendency/hypertrophic or keloidal scarring on the face due to acne
- Facial scars due to reasons other than acne like varicella, trauma, burns etc

- Collagen vascular disease, bleeding disorders
- Any active bacterial , fungal or viral infection over face
- Pregnant and lactating females
- Known hypersensitivity to tazarotene
- Age less than 18 years
- On anticoagulant therapy or aspirin

You will be one of the patients we plan to recruit in this study. You will be instructed to apply 0.1% tazarotene gel over one half of the face and dermaroller will be done on other half of the face for a total of four sittings at monthly interval.

What is the purpose of this research?

The purpose of this research is to compare the efficacy of microneedling versus topical tazarotene 0.1% gel in the management of moderate to severe atrophic acne scars.

Post acne scarring is a common complication of acne. Cosmetic appearance of the post acne facial scarring can be improved by various methods. Topical tazarotene 0.1% gel is an effective medical method in the management of post acne scars. Among the procedural methods microneedling with dermaroller is a novel and a promising option. It is a minimally invasive day care procedure for the management of atrophic acne scars.

Information obtained from this study would be beneficial to other patients with atrophic post acne scarring.

The study design

In this split-face design, the face of each patient will be randomized for microneedling on one side and topical tazarotene gel on opposite side. Randomisation will be done using computer generated random number table.

Study Procedure

You should apply 0.1% tazarotene gel as a thin film over one half of the face once daily in the evening daily for 3 continuous months. It should be applied approximately 15 to 20 minutes after washing your face in the evening by placing a pea-sized amount in the palm of your hand and, using the tip of a finger to cover the entire half of face. If you experience facial dryness you can use a moisturizing cream during the day (entire face), but the use of any other lotions, creams, medicated powders, or solutions on the face is prohibited. You should follow strict photo protective measures including application of broad spectrum sunscreen of SPF 30 during the entire study period.

Dermaroller will be done on other half of the face for a total of three sittings at monthly interval. You should come to minor operation theatre in OPD on 3 days at monthly interval for the procedure. The procedure will be done under local anaesthesia under strict aseptic precautions. Dermatologic examination and photographic evaluation of your face will be done during the study.

You may have to come to the hospital for examination apart from your scheduled visits, if required.

Women of childbearing potential

You must not participate if you are pregnant, breastfeeding a child, or if you are of childbearing potential and not practicing two forms of effective methods of contraception. These forms could be either an oral contraceptive pill plus a condom or diaphragm; or two barrier methods (e.g. a condom and diaphragm). You may also consider participating, if you are surgically sterile or postmenopausal. If you become pregnant during the study, your unborn child may be exposed to risks.

Possible benefits to you

You will be getting treatment benefit along with dermaroller sessions.

Possible risks to you

Common adverse effects of topical tazarotene are erythema, burning/stinging, itching, and dryness.

Side effects that have been reported with dermaroller include procedural pain, transcient post procedure erythema, bruising and swelling, PIH and tram-track scarring. Most of these were mild in nature. PIH was mainly due to inadequate sun protection.

Compensation

You will not receive any compensation for the inconvenience and travel.

Possible benefits to other people

The results of the research may provide benefits to the society in terms of advancement of medical knowledge and/or therapeutic benefit to future patients.

The alternatives you have

If you do not wish to participate, you have the alternative of getting the standard treatment for your condition.

Cost to the participant

You will be required to pay for the medications and lab tests. You will not be paid to participate in this research study.

What should you do in case of injury or a medical problem during this research study?

Your safety is the prime concern of the research. If you are injured or have a medical problem as a result of being in this study, you should contact the person listed at the end of the consent form. You will be provided the required care/treatment.

You will be entitled to your legal rights besides this.

Confidentiality of the information obtained from you

The identity status of the participants shall be kept confidential.By signing this document, you will be allowing the research team investigators, other study personnel, institutional ethics

committee and any person or agency required by law like the Drug Controller General of India to view your data, if required. The information from this study, if published in scientific journals or presented at scientific meetings, will not reveal your identity.

How will your decision to not participate in the study affect you?

Your decision not to participate in this research study will not affect your medical care or your relationship with the investigator or the institution. Your doctor will still take care of you and you will not lose any benefits to which you are entitled.

Can you decide to stop participating in the study once you start?

You are free to withdraw your consent and to stop participating in this research study at any time. It will have no effect on your treatment.

Can the investigator take you off the study?

You may be taken off the study without your consent if you do not follow instructions of the investigators or the research team or if the investigator thinks that further participation may cause you harm.

Right to new information

If the research team gets any new information during this research study that may affect your decision to continue participating in the study, or may raise some doubts, you will be told about that.

Contact person

For further information/ questions, you can contact us at the following address:

Dr. Afra T P

Phone No- 8427652806

Department of Dermatology, Venereology and Leprology,

PGIMER, Chandigarh